II. REMARKS

Formal Matters

Claims 21-24 are pending.

Claims 1-20 have been canceled from the application.

No new matter has been added.

35 U.S.C. §103 Rejection over Rowe

The claims have been rejected as being obvious over Rowe. The rejection is traversed in view of the attached publications and the arguments put forth below.

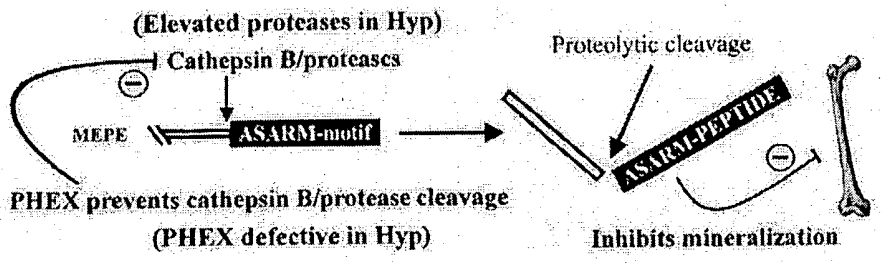
Applicants have claimed a formulation comprised of a carrier and any one of four specific peptide sequences. The Examiner has correctly pointed out that these specific peptide sequences are part of the larger sequence which is disclosed by Rowe. In essence, the rejection argues that smaller sequences disclosed by Rowe are obvious in view of Rowe and would be expected to enhance bone growth at the same level because the claimed sequences include RGD as part of the sequence. However, the literature does not support this position.

Rowe discloses the entire sequence which is referred to as the matrix extracellular phosphoglycoprotein (MEPE). Applicants have attached hereto a copy of a recently published article from the "Journal of Bone and Mineral Research" in vol. 19, published November 3, 2004. This article shows that one of the peptides claimed as part of independent claim 21 and indicated as a SEQ ID NO.:47 does provide potent *in vitro* and *in vivo* bone formation activities. The paper also shows that by disrupting the RGD sequence these activities are lost. Thus, the authors conclude that stimulating activities of osteoblasts (bone formation cells) by this peptide are attributed to the RGD sequence.

To a degree, this paper supports the Examiner's position. However, the full length MEPE molecule also includes the RGD sequence. Applicants have attached hereto a paper published in "Bone" at vol. 34, 2004. This paper shows that the full length MEPE molecule actually inhibits osteoblast activity. Specifically, the paper shows that MEPE inhibits BMP-2 mediated osteoblast mineralization.

If some sequences which include the RGD stimulate bone formation and others inhibit bone formation those skilled in the art can not know that one sequence will have a desired effect.

Below is a graphic representation of how the MEPE actually inhibits mineralization. The graphic representation is taken directly from the published article attached hereto.



Based on the above it is applicants' position that the MEPE molecule (which includes an RGD) disclosed by Rowe does not render obvious all of the smaller sequences (which include an RGD) contained within MEPE. Specifically, some sequences within MEPE such as those claimed by applicants provide improved results whereas other sequences provide adverse effects and both include an RGD. The results with sequences comprises an RGD giving opposing positions are supported by the attached publications.

Applicants point out that individuals named as co-inventors on the present application are named as co-authors on the attached publications.

35 U.S.C. §103 Rejection over Rowe in combination with Cerny et al.

Claims 23 and 24 were rejected as obvious over the combination of Rowe in view of Cerny et al. The rejection is traversed.

Nothing within Cerny et al. suggests the particular sequences claimed by applicants. Further, as indicated above Rowe does not suggest these sequences. The attached publications support applicants position that different sequences comprising RGD could provide desirable or undesirable results with regard to promoting bone growth. In view of such, even if Rowe and Cerny et al. are combined they do not teach towards the particular sequences which promote bone growth. Still further they do not teach towards the use of those particular sequences in formulations for a toothpaste or a mouthwash.

As shown within the "Bone" article attached. Certain sequences from MEPE could be included within the toothpaste or mouthwash and actually inhibit mineralization. This would be particularly undesirable in a mouthwash or toothpaste. In view of such the rejection should be reconsidered and withdrawn.

CONCLUSION

The Examiner has correctly pointed out that Rowe teaches MEPE. However, the attached

publications show that particular sequences within MEPE can be beneficial or undesirable. The publication in the "Journal of Bone and Mineral Research" shows that the peptide of SEQ ID NO.: 47 gives particularly desirable results. The publication in "Bone" shows that not all sequences within MEPE provide desirable results and some can actually inhibit mineralization even though the RGD is present. In view of such the particular sequences within the formulation claimed by applicants are not obvious in view of Rowe. Accordingly, reconsideration and withdrawal of the rejections and allowance of the application is respectfully requested.

In the event the Examiner finds that minor issues remain unresolved the Examiner is respectfully requested to contact the undersigned attorney at the indicated telephone number to arrange for an interview to expedite the disposition of this application. In the event additional petitions are required including additional extensions the applicants petition for any required relief and authorize the Commissioner to charge the costs of such petitions to our Deposit Account No. 50-0815, Attorney Docket No. BEAR-006.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: 8/DEC/04

By: _____
Karl Bozicevic
Registration No. 28,807

Encl.: Rowe et al., *Bone,* 34:303-319 (2004)
Hayashibara et al., *Journal of Bone and Mineral Research,* 19:1-8 (2004).

BOZICEVIC, FIELD & FRANCIS LLP
1900 University Avenue, Suite 200
East Palo Alto, CA 94303
Telephone: (650) 327-3400
Direct: (650) 833-7735
Facsimile: (650) 327-3231

F:\DOCUMENT\BEAR (formerly 8302)\006\amend to oa 08-16-04.doc